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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/720,096	02/01/2001	Dan Nilsson	54337.000009	6906

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EXAMINER	
STEADMAN, DAVID J	
ART UNIT	PAPER NUMBER
1652	17

DATE MAILED: 01/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/720,096	NILSSON ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *18-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17 and 24-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Application Status

Claims 1-32 are pending in the application.

Applicants' amendment to the specification and claims 1, 4, 5, 7, 8, 10-12, 17, 18, 23, 26, and 27 and addition of claims 28-31 in Paper No. 12, filed 08/27/02, is acknowledged.

Receipt of a Declaration under 37 CFR 1.132 by inventor Nilsson and filed as Paper No. 13 is acknowledged.

Applicants' amendment to claims 1, 3, 18-22, 26, 27, and 31 in Paper No. 14, filed 09/30/02, is acknowledged.

Applicants' amendment to claims 9 and 23 and addition of claim 32 in Paper No. 15, filed 10/22/02, is acknowledged.

Receipt of a Declaration of Biological Deposit Under the Budapest Treaty filed as Paper No. 16 is acknowledged.

Applicants' arguments presented in Paper Nos. 12, 14, and 15 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Lack of Unity

1. In Paper No. 11, the examiner held that a lack of unity does not exist between Groups I and II as set forth in Paper No. 8. The examiner initially applied the reference of Richardson (J Dairy Sci 66:2278-86) to demonstrate the method of Group I was known in the prior art. However, applicants traversed the lack of unity of Paper No. 8 asserting Richardson does not teach the method of Group I. Upon review of the reference of Richardson, it became apparent to the examiner that Richardson does not teach the method of Group I. The examiner next applied the references of Johansen et al. (*Dev Biol Stand* 85:531-

34) and Dickely et al. (*Mol Microbiol* 15:839-847) to demonstrate that the modified lactic acid bacterium of Group II was known in the art at the time of the invention. The lack of unity was maintained based on these references without making the lack of unity final.

In the instant response, applicants continue to traverse the lack of unity. Applicants argue (beginning at page 7 of Paper No. 12) that the purine auxotroph of Johansen is capable of growing in the absence of purine in a medium and that neither of the cited references discloses or suggests that auxotrophic lactic acid bacterial strains retain their metabolic activity when cultured in a medium lacking the compound for which the bacterial strains require for growth. Applicants further argue (beginning at page 2 of Paper No. 15) that because claims 18 and 19 are patentable in view of Johansen et al. and Dickely et al., claims 18 and 19 of Group II share a special technical feature with the claims of Group I as the claims of Group I are methods of using the claims of Group II. Applicants argue that unity of invention was satisfied during the international search and preliminary examination report. Applicants' arguments are not found persuasive. Regarding applicants' arguments in Paper No. 12, the purine auxotroph of Johansen is disclosed as being capable of growth in a purine-free medium *only in the presence of the ochre suppressor* (see page 533, third paragraph). Therefore, in the absence of the ochre suppressor, the purine auxotroph of Johansen would not grow in a purine-free medium, thus the name "purine auxotroph". Dickely similarly teach a purine auxotroph (see page 842). The ability of the auxotrophic strains of Johansen and Dickely would inherently have had the ability to retain their metabolic activity when cultured in a medium lacking the compound for which the bacterial strains require for growth. Applicants are advised that if applicants present evidence that the strains of Johansen and Dickely are not able to retain their metabolic activity when cultured in a medium lacking the compound for which the bacterial strains require for growth, this evidence may be used against applicants in a scope of enablement rejection under 35 USC 112, first paragraph. Regarding applicants' arguments in Paper No. 15, the examiner has made no indication that claims 18 and 19 are patentable. In fact, the examiner has not examined claims 18 and 19 to determine their patentability as these claims have been withdrawn from consideration as being drawn to a non-elected invention. It is noted that the

examiner is not bound by the international search report or preliminary opinion. In other words, even though unity of invention was found to be satisfied during the international search and preliminary examination report, the examiner at his discretion may require an election to a single invention due to a finding of a lack of unity.

The requirement is still deemed proper and is therefore made FINAL.

Claims 18-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim.

Claims 1-17 and 24-32 are being examined on the merits.

Claim Objections

2. Claims 24 and 25 remain objected to as being dependent upon non-elected claims. It is suggested that applicants incorporate the limitations of claims 18 and 21 into claim 24.

Claim Rejections - 35 USC § 112, Second Paragraph

3. Claims 1-17, 26, and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. The rejection of claim 1 (claims 2-17, 26, and 27 dependent therefrom) as being unclear in the recitation of "attack by bacteriophages" is maintained for the reasons of record and the reasons described below. The rejection was fully explained in a previous Office action. Applicants argue the term "not susceptible to attack by bacteriophages" is clearly defined in the specification at page 6 and therefore, the claim is definite. Applicants' argument is not found persuasive. The definition of "not susceptible to attack by bacteriophages" as provided in the specification is as follows: "includes the capability of a host cell to be metabolically active even though a bacteriophage adsorbs to the host cell surface and injects its DNA into the host cell" (page 6). While a definition of the term has been provided, the meaning of the term "not susceptible to attack by bacteriophages" is not limited to this definition and it remains unclear

as to the meaning of the term. One of skill in the art would recognize that the term has multiple meanings. For example, in addition to the open-ended definition provided in the specification, the term can be interpreted as a bacterial culture that is resistant to bacteriophage infection. Thus, one of skill in the art would not recognize the meaning of the term. It is suggested that applicants clarify the meaning of the term.

Claim Rejections - 35 USC § 112, First Paragraph

5. The written description rejection of claims 1-3, 6-19, 21-27, and 30-32 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons described below. The rejection was fully explained in a previous Office action (see pages 5 and 6 of Paper No. 11). Applicants argue (beginning at page 10 of Paper No. 12) the Office action attempts to limit the claims to a method using an auxotrophic lactic acid bacteria, milk as a substrate, and a bacteria with a single genetic modification. Applicants argue this is improper as the specification provides adequate written description of the genus of bacterial cultures as recited in the claims. Applicants assert that at the time of filing, a skilled artisan would recognize applicants possessed the claimed invention. Applicants argue the specification satisfies the written description requirement without utilizing any particular form of the disclosure and applicants have chosen to claim their invention generically based on a written description of specific examples of the recited genus of bacterial cultures. Applicants summarize their argument by stating that, at the time of the invention, applicants were in possession of the claimed invention. Applicants' arguments are not found persuasive. Regarding claims 1-3, 6-17, and 24-32, the specification does not provide adequate written description of the genus of recited bacterial cultures. The specification has provided only two species of the recited genus of bacterial cultures, i.e., a purine or thymidine auxotrophic mutant bacterium, which is insufficient to provide a description of the entire genus of recited bacterial cultures. Specifically regarding claims 12-14, the specification does not provide adequate written description of the genus of recited genetically modified bacterial strains. The specification has provided only two species of the recited genus of modified bacterial strains, i.e., a purine or thymidine auxotrophic mutant bacterium

overexpressing F1-ATPase, which is insufficient to provide a description of the entire genus of modified bacterial strains. Specifically regarding claims 15 and 16, the specification does not provide adequate written description of the genus of recited conditional mutants. The specification has provided only two species of the recited genus of conditional mutants, i.e., a purine or thymidine auxotrophic mutant bacterium, which is insufficient to provide a description of the entire genus of recited conditional mutants. The functional recitation of being a bacterial culture that is not capable of DNA replication, RNA transcription, or protein synthesis in a substrate material, but are capable of modifying said substrate material is insufficient to provide an adequate written description as the genus encompasses widely variant species. The disclosed purine or thymidine *L. lactis* mutants do not represent a representative number of species within the recited genus as one of skill in the art, based on the species encompassed by the genus, would recognize there is *substantial* variation of species within the genus. When there is substantial variation of species within the genus, the specification should describe a sufficient number of species to reflect the variation within the genus. In the instant case, the disclosure of only the species as described above is not a representative number of species within the recited genus. What represents a "representative number" is inversely related to the skill and knowledge in the art. At the time of the invention, methods for using bacterial cultures that are not capable of DNA replication, RNA transcription, or protein synthesis in a substrate material, but are capable of modifying said substrate material were not common in the art. As such, more evidence is required to show possession of the claimed invention. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

6. The enablement rejection of claims 1-17 and 24-32 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons described below. The rejection was fully explained in a previous Office action (see pages 6-9 of Paper No. 11). Applicants argue (beginning at page 13 of Paper No. 12) this rejection appears to attempt applicants to impermissibly limit their invention to the disclosed examples. Applicants argue that the specification enables those skilled in the art to make the

entire scope of the claimed invention. Applicants' arguments are not found persuasive. Undue experimentation would be required for a skilled artisan to make the entire scope of the claimed invention. Factors to be considered in determining whether undue experimentation is required, are summarized in *In re* Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s). Applicants have provided insufficient guidance to enable a skilled artisan to make and use the entire scope of recited bacterial cultures, genetically modified bacterial strains, and conditional mutants. The specification provides guidance only for generation of two working examples of bacterial cultures that are not capable of DNA replication, RNA transcription, or protein synthesis in a substrate material, but are capable of modifying said substrate material, i.e., a *Lactococcus lactis* purine auxotroph and a *Lactococcus lactis* thymidine auxotroph with the ability to acidify milk in the absence of purine or thymidine, respectively (see Examples 1 and 2). It is noted that the Declaration of inventor Nilsson demonstrates acidification of a culture medium using a *L. lactis* thymidine auxotroph (see Paper No. 16). However, it is unclear as to the usefulness of acidifying a culture medium by the production of lactic acid using said auxotroph as neither the specification, the prior art, or the Declaration by inventor Nilsson indicates that such acidification of *any* substrate would be so useful. Furthermore, while purine and thymidine auxotrophs are known in the art, neither the specification nor the prior art provides further guidance as to the construction of other bacterial cultures that are not capable of DNA replication, RNA transcription, or protein synthesis in a substrate material, but are capable of modifying said substrate material. It is noted that auxotrophic bacterial strains are known in the art - for example, Herrington et al. (J Bacteriol 157:126-129) teach an E. coli thymidine auxotroph. However, it is not clear as to what substrates this strain would be useful in modifying. Thus, while auxotrophic bacterial strains other than *L. lactis* are known in the art, the specification has not provided guidance as to how to use other bacterial strains or any other strains that are not capable of DNA replication, RNA transcription, or protein

synthesis in a substrate material, but are capable of modifying said substrate material it is not clear that these strains will be so useful for modifying a substrate material. Neither the specification nor the prior art provides guidance as to the range of substrates that can be modified using any bacterial culture that is not capable of DNA replication, RNA transcription, or protein synthesis in a substrate material, but is capable of modifying said substrate material. The use of purine or thymidine auxotrophs or any other bacterial cultures that are not capable of DNA replication, RNA transcription, or protein synthesis in a substrate material, but are capable of modifying said substrate material for modifying milk or any other substrates was not common in the art at the time of the invention and therefore, guidance in this regard should be provided in the specification. While applicants have demonstrated that *L. lactis* purine and thymidine auxotrophs are capable of producing lactic acid in milk (see Examples 1 and 2) and culture media supplemented with lactose (see Declaration by inventor Nilsson in Paper No. 13), this guidance does not enable a skilled artisan to alter *all* substrates and the guidance necessary to practice the claimed invention using *any* substrate has not been provided in the specification. Thus, based on the state of the art and the level of skill in the art, a skilled artisan would recognize the high degree of unpredictability in using any bacterial culture that is not capable of DNA replication, RNA transcription, or protein synthesis for modifying any substrate material as broadly encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claimed invention. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re* Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re* Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 103

15. All rejections under 35 USC 103(a) are withdrawn for the following reasons. While Dickely teaches purine auxotrophs of *L. lactis* and that milk contains insufficient amounts of purine or pyrimidine

nucleotides to support the growth of purine or pyrimidine auxotrophs of lactic acid bacteria, the examiner can find no teaching or suggestion in the prior art of record that such *L. lactis* purine auxotrophs would be able to acidify milk, even if the milk were contaminated with phage. Furthermore, the examiner can find no teaching or suggestion to motivate one of ordinary skill in the art to use the *L. lactis* purine auxotroph of Dickely for acidification of milk. It is noted that Herrington et al. (J Bacteriol 157:126-129) teaches that an *E. coli* thymidine auxotrophic strain has the ability to suppress nonsense mutations induced by bacteriophage T4 (page 126, abstract). However, there is no indication in the reference of Herrington to suggest that the metabolic activity of their mutant is substantially unaffected by bacteriophage. Furthermore, there is no indication that a thymidine auxotroph of *L. lactis* would maintain the ability to acidify milk in the presence of bacteriophage. Thus, the cited references do not provide a motivation for using the *L. lactis* purine auxotrophs of Dickely for the acidification of milk.

Conclusion

19. All claims are rejected. No claim is in condition for allowance.

20. The examiner requests that applicants provide a copy of all pending claims in the response to this Office action.

Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally be reached Monday-Thursday from 6:30 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX number for this Group is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.
Patent Examiner
Art Unit 1652

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